REMARKS

Allowable Subject Matter

In the May 28, 2004 Office Action, Examiner Davis found claim 26 to be free of prior art and to meet all requirements of patentability. In the October 21, 2004 Office Action, the allowability of this claim was withdrawn.

Rejections of Claims and Traversal Thereof

In the October 21, 2004 Office Action,

claims 1-2, 20 and 26-28 were rejected under 35 U.S.C. §112, first paragraph.

This rejection is hereby traversed, and reconsideration of the patentability of amended claims herein is requested, in light of the ensuing remarks.

Rejection under 35 U.S.C. §112, first paragraph

According to the Office, claims 1-2, 20 and 26-28 contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is mostly connected, to make and/or use the invention. Initially, it should be noted that the rejection by the Office provides no guidance as to why the claims do not meet the requirements of 35 U.S.C. §112, first paragraph. For example, is the specification not commensurate in scope with these claims or is undue experimentation required? Applicant should not have to guess why the claims do not meet the enablement requirements of 35 U.S.C. §112, first paragraph.

Claim 1 of the present invention reads as follows:

1. An isolated polypeptide that induces cell death *in vitro* consisting of SEQ ID NO: 8.

The test for enablement is whether one skilled in the art could make and use the claimed invention from the disclosure coupled with information known in the art without undue experimentation. See *United States v. Telectronics, Inc.*, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988), cert. denied, 109 S.Ct. 1954 (1989);

In re Stephens, 188 USPQ 659, 661 (CCPA 1976). In making a rejection on the ground of nonenablement, the Office has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. See *In re Wright*, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). A disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. If the Office doubts the results shown in the application then it is incumbent upon the Patent Office, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. *In re Marzocchi*, 169 USPQ 367, 369 (C.C.P.A. 1971).

In the October 21, 2004 Office Action, the Office states that the "specification discloses that the polynucleotide encoding SEQ ID NO: 8 could induce programmed cell death in vitro, when transfecting into human cell lines (Example 2, pages 42-43)." The Office then goes on to state that:

> "One cannot extrapolate the teaching in the specification to the enablement for scope of the claims. Although SEQ ID NO: 8 could kill cells in vitro, one cannot predict that SEQ ID NO: 8 could be used in vivo for treating or preventing a diseases [sic] having an increase or decrease in proliferation, because conditions in vitro and in vivo are not the same."

Applicant questions as to whether the Office is making reference to the claims submitted on July 28, 2004 because the claims were amended to recite *in vitro* methods and none of the claims could possibly be read to include *in vivo* use. Applicant has reviewed the "TRAINING MATERIALS FOR EXAMINING PATENT APPLICATIONS WITH RESPECT TO 35 U.S.C. SECTION 112, FIRST PARAGRAPH-ENABLEMENT CHEMICAL/BIOTECHNICAL APPLICATIONS" as available to patent examiners and applicants on the USPTO web site at http://www.uspto.gov/web/offices/pac/dapp/1pecba.htm#7e and submits that all pending claims meet the requirements describes in this training material.

Specifically, applicant reviewed Examples 5E (Protein to treat Obesity) and G (Gene Therapy) because these examples were closest to the presently claimed invention. A copy of the relevant text of the "Training Material" relative to Examples 5E and G is included in Appendix A.

As stated above and in agreement with the Office, applicant has disclosed an isolated polypeptide having an amino acid sequence of SEQ ID NO: 8, which has been described in the specification. Applicant has included an *in vitro* example showing the effectiveness of this expressed protein in the induction of cell death. With guidance from the "Training Materials," applicant reviewed the present specification and submits that it discloses the polypeptide and its sequence and also provides sufficient enablement for using said polypeptide *in vitro* for providing the desired biological action in the cells. Further, the specification provides ample guidance to insert the polynucleotide, which encodes the polypeptide of SEQ ID NO: 8, into a cell line for expression therein. Applicant has described several applicable vectors, acceptable host cells and methods of transfection in the specification (See page 25 to 34 of the specification). Furthermore, the knowledge of one skilled in the art is so sophisticated that inserting a nucleotide sequence into an expression vector is certainly within the capabilities of one skilled in the art. Expressing a polynucleotide is no longer considered an unpredictable art, and as such, the details of inserting the polynucleotide and expressing same in a cell should not have to be explained in exhausting detail. The specification includes an *in vitro* working example with the polypeptide of interest (SEQ ID NO: 8) and this example demonstrates that the protein of interest, when expressed, increases the level of cell death.

As stated above, claims 1 and 20 recite a polypeptide of SEQ ID NO: 8 that induces cell death. Since this claim recites an "enabled use," it is sufficient to preclude an enablement rejection. The state of the art at the time of filing was such, that it is well known to insert polynucleotides in cells *in vitro* for production of a preferred protein. As stated above, the specification discloses an *in vitro* use for inducing cell death and clearly discloses how to make and use the polypeptide in the *in vitro* environment.

In the G example (Gene Therapy) of the "Training Material," it was found that *in vitro* examples were not sufficient to show *in vivo* effectiveness. However, the "Training Material" clearly stated that if the claims were amended to recite an in vitro method, the claims met the enablement requirements.

For example, the following claims 2 and 3 were found enabling.

> 2.. A composition comprising the viral vector of claim 1 and a carrier.
> 3. A method for introducing a gene of interest into a cell *in vitro* comprising contacting said cell with the viral vector of claim 1.

Clearly, applicant's claims 2 and 27 are enabling because they are exactly as that found to meet the enablement requirement in the "Training Material." Applicant will address the method claims further in this discussion.

Reviewing the "Training Materials" relative to Example 5E provides further evidence that applicant's claims 1 and 26 meet the enablement requirements because the sequence is disclosed in the specification and an enabled use is also disclosed. Claims 2 and 27 also meet the enablement requirements because as stated in the "Training Material," " removing 'pharmaceutical' and 'pharmaceutically acceptable' from claims 3-4 would overcome the rejection of these claims since one would know how to use such compositions as additives in animal feed as disclosed in the specification." Applicant has removed the word "pharmaceutically" from the claims and because one skilled in the art, after reading the present specification, would know that this polypeptide induces cell death, the claims meet all the requirements of enablement.

The method claims recite all the limitations of the product claims. Specifically, claim 13 recites an *in vitro* method for screening compounds. When this claim is read in light of the specification and the state of the prior art, it covers methods for use in assays. The specification provides sufficient guidance for testing a test compound relative to the polypeptide (SEQ ID NO: 8) without undue experimentation. Example 2, as described in the present specification, can be easily recreated with the addition of a test compound.

The Office contends that variants of SEQ ID NO: 8 as recited in claims 20 and 28 do not meet the enablement requirements of 35 U.S.C. §112, first paragraph. Again, applicant is concerned as to whether the Office is reviewing the amended claims submitted on July 28, 2004. The Office makes reference to "at least 90% identity to SEQ ID NO: 8," however in the July 28, 2004 the claim 20 was amended to variants of SEQ ID NO. 8 that must include at least the following limitations:

(1) at **least 95% identity** to SEQ. ID NO. 8,
(2) a conserved carboxy end region having an amino acid sequence of amino acid residues 353 to 405 of SEQ ID NO. 8,
(3) conservative changes in any amino acid substitutions and
(4) induces cell death *in vitro*.

The issue raised by the Office seems to relate to whether one skilled in the art could make and use the claimed invention without undue experimentation. Applicant submits that the question of undue experimentation is a matter of degree. The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation "must not be unduly extensive." *Atlas Powder Co., v. E.I. DuPont de Nemours & Co.*, 224 USPQ 409, 413 (Fed. Cir. 1984). The Patent and Trademark Office Board of Appeal summarized the point well when it stated:

> "The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed." *Ex parte Jackson*, 217 USPQ 804, 807 (1982).

Here, all the Office has established is that some experimentation would be required to make and use other embodiments of the claimed invention. What the Office has not done is to perform the fact-finding needed in order to reach a proper conclusion of undue experimentation. The specification provides ample guidance for testing variant proteins that meet the criteria set forth in claim 20 and 28. It should be noted that claim 20 clearly defines parameters that enable broader protein claims because the claim recites functional language that clearly defines the variant protein and its activity. According to the court in *In re Marks*, 12 USPQ2d 1904 (BPAI 1989) with the addition of functional language, one skilled in the art would be able to determine in a routine fashion, without undue experimentation whether the protein would result in inducing cell death. Clearly, the recited parameters encompass a limited amount number of variants.

The biological activity, that being, the ability to induce cell death can be very easily determined by one skilled in the art, and the specification provides guidance as set forth in Example 2. Thus, the breath of the claims is not broader than that described in the specification and the quantity of experimentation to practice the full scope of the claims does not require undue experimentation. The specification provides guidance regarding how to make and use a functional variant. Clearly, the level of skill in this field is very high and one skilled in the art is very aware of conservation substitutions of amino acid residues. As such, information known by one skilled in the art will provide ample assistance in practicing the claimed invention, and as such, known prior art contributes significantly to the enabling scope of the disclosure. Moreover, as stated by the Office at page 35 of the December 11, 2003 Office Action, Sambrook, et al. provides methods for elucidating structure-function relationships by analyzing the properties of normal and mutant proteins.

The Office has cited numerous references to illustrate that a change in an amino acid, even with a conservative substitution, can alter the function of the protein. However, what the Office is missing from this analysis is that the functionality of the variant protein is included in the claim, and one skilled in the art can easily test to determine if the variant protein increases cell death. Further, it should be noted that there is no rule that the level of activity must be the same for all substitutions to meet the requirements of 35 U.S.C. §112, first paragraph, and one skilled in the art can easily determine the activity and choose the most effective variant.

The Office makes further reference to the fact that the claims, as written, include amino acid sequences that may include additions or deletions of amino acid residues. Applicant stresses that even if the 5% difference between SEQ ID NO: 8 and the variant protein includes deletions or additions of amino acid residues, the protein still must effect increased cell death and this functionality can be determined without undue experimentation.

Applicant submits that on this very day of January 18, 2005 a patent issued with claims as follows:

US006844323B2

(12) **United States Patent**
Mao et al.

(10) **Patent No.: US 6,844,323 B2**
(45) **Date of Patent: Jan. 18, 2005**

(54) **POLYPEPTIDE-CALCITONIN 11 AND THE POLYNUCLEOTIDE ENCODING IT**

(75) Inventors: Yumin Mao, Shanghai (CN); Yi Xie, Shanghai (CN)

(73) Assignee: BioWindow Gene Development Inc., Shanghai (CN)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 407 days.

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(52) U.S. Cl. 514/12; 530/324

(58) Field of Search 514/12; 530/324

(56) References Cited

PUBLICATIONS

DNA Res. 6(1), 63–70 (1999), Nagase T., et al., *Prediction of the sequences of unidentified human genes. XIII. The complete sequences of 100 new cDNA clones from brain which code for large proteins in vitro.*
Genome Res. 9(3), 242–250 (1999), Rebout, J., Et al., *Comparative genomic analysis of the interferon/interleukin–10 receptor gene cluster.*

Primary Examiner—Robert A. Wax
(74) *Attorney, Agent, or Firm*—Crowell & Moring LLP

(57) **ABSTRACT**

The present invention discloses a new polypeptide-calcitonin 11, the polynucleotide encoding it and a method producing the polypeptide by recombinant DNA technology. The present invention further discloses a method using the polypeptide to treat various disorders, e.g. malignant neoplasm, hematopathy, HIV infection and immunological disease and various inflammation etc. The present invention also discloses agonists of the polypeptide and their therapeutic uses. The present invention further discloses the use of the polynucleotide encoding the new calcitonin 11.

4 Claims, 1 Drawing Sheet

We claim:

1. An isolated polypeptide having a calcitonin 11 activity and comprising an amino acid sequence of SEQ ID NO: 2.

2. An isolated polypeptide having a calcitonin 11 activity and comprising an amino acid sequence that is at least 95% identical to SEQ ID NO: 2.

3. A method for detecting a disease related to the polypeptide of claim 2, or for determining a susceptibility of a mammal thereto, said method comprising detecting the amount of expression of said polypeptide, or detecting the activity of said polypeptide.

4. A pharmaceutical composition comprising a polypeptide according to claim 2, and a pharmaceutically acceptable carrier.

* * * * *

Claim 2 that issued in this patent is comparable to claims 20 and 28 and after a thorough review of the specification in this issued patent, it is evident that applicant's specification provides similar guidance for practicing the present invention. Applicant is well aware that patentability of a claim is not controlled by the fact that similar claims have been allowed in the Patent Office, since each claim must be patentable in

its own right. However, as stated by the Court in *In re Bisley*, 954 USPQ 80, 83 (CCPA 1952) similar claims allowed by the Patent Office Tribunals furnish evidence of what features those tribunals regarded as patentable, and the court determined it was proper and in fact sometimes necessary to consider allowed claims in order to fully determine the views of the board and the examiner.

Applicant submits that the instant application provides sufficient and enabling information for a person of ordinary skill in the art to practice applicant's invention and respectfully requests the withdrawal of all rejections under §112, first paragraph.

Rejoining of Method Claims

Applicant is requesting that all method and use claims that are currently withdrawn be rejoined and examined according to the guidelines set forth in Section 821.04 of the MPEP.

Conclusion

Applicant has satisfied the requirements for patentability. All pending claims are free of the art and fully comply with the requirements of 35 U.S.C. §112. It therefore is requested that Examiner Davis reconsider the patentability of all pending claims in light of the distinguishing remarks herein, and withdraw all rejections, thereby placing the application in condition for allowance. Notice of the same is earnestly solicited. In the event that any issues remain, Examiner Davis is requested to contact the undersigned attorney at (919) 419-9350 to resolve same.

Respectfully submitted,

Marianne Fuierer
Reg. No. 39,983
Attorney for Applicant

INTELLECTUAL PROPERTY/ TECHNOLOGY LAW
P.O. Box 14329
Research Triangle Park, NC 27709
Phone: (919) 419-9350
Fax: (919) 419-9354
Attorney Ref.: 4115-131